CLAIMS

What is claimed is:

1. A method of treating, preventing, delaying the onset of, or reducing the effects of proinflammatory cytokines in a mammal comprising the steps of administering a therapeutically effective amount of at least one tissue protective cytokine in a pharmaceutical carrier.

2. The method of claim 1, wherein the at least one tissue protective cytokine comprises a chemically modified erythropoietin or mutated erythropoietin.

3. The method of claim 2, wherein the the chemically modified erythropoietin is selected from the group consisting of i) an erythropoietin that lacks sialic acid moieties, ii) an erythropoietin having at least no sialic acid moieties; iii) an erythropoietin having at least no N-linked or no O-linked carbohydrates; iv) an erythropoietin having at least a reduced carbohydrate content by virtue of treatment of native erythropoietin with at least one glycosidase; v) an erythropoietin having at least one or more oxidized carbohydrates; vi) an erythropoietin having at least one or more oxidized carbohydrates and is chemically reduced; vii) an erythropoietin having at least one or more modified arginine residues; viii) an erythropoietin having at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule; ix) an erythropoietin having at least a modified tyrosine residue; x) an erythropoietin having at least a modified aspartic acid or a glutamic acid residue; xi) an erythropoietin having at least a modified tryptophan residue; xii) an erythropoietin having at least one amino group removed; xiii) an erythropoietin having at least an opening of at least one of the cystine linkages in the erythropoietin molecule; or xiv) a truncated erythropoietin.

4. The method of claim 3, wherein the chemically modified erythropoietin lacks

erythropoietin's erythropoietic effects.

5. The method of claim 4, wherein the chemically modified erythropoietin comprises carbamylated erythropoietin.

6. The method of claim 2, wherein the mutated erythropoietin is selected from the group consisting of one or more of the following mutations C7S, R10I, V11S, L12A, E13A, R14A, R14B, R14E, R14Q, Y15A, Y15F, Y15I, K20A, K20E, E21A, C29S, C29Y, C33S, C33Y, P42N, T44I, K45A, K45D, V46A, N47A, F48A, F48I, Y49A, Y49S, W51F, W51N, Q59N, E62T, L67S, L70A, D96R, K97D, S100R, S100E, S100A, S100T, G101A, G101I, L102A, R103A, S104A, S104I, L105A, T106A, T106I, T107A, T107L, L108K, L108A, S126A, F142I, R143A, S146A, N147K, N147A, F148Y, L149A, R150A, G151A, K152A, L153A, L155A, C160S, I6A, C7A, B13A, N24K, A30N, H32T, N38K, N83K, P42A, D43A, K52A, K97A, K116A, T132A, I133A, T134A, K140A, P148A, R150B, G151A, K152W, K154A, G158A, C161A, and/or R162A.

7. The method of claim 6, wherein the mutated erythropoietin lacks erythropoietin's erythropoietic effects.

8. The method of claim 1 wherein the proinflammatory cytokine comprises an Interleukin or TNF.

9. The method of claim 8 wherein the proinflammatory cytokine is TNF.

10. The method of claim 1 wherein the effect of the proinflammatory cytokine comprises fever, wasting, lethargy, anemia, edema, ischemia, organ failure and insulin resistance.

11. A method of treating, preventing, delaying the onset of a condition associated with an effect of proinflammatory cytokines in a mammal comprising the steps of administering a therapeutically effective amount of at least one tissue protective cytokine in a pharmaceutical carrier.

12. The method of claim 11, wherein the at least one tissue protective cytokine comprises a chemically modified erythropoietin or mutated erythropoietin.

13. The method of claim 12, wherein the the chemically modified erythropoietin is selected from the group consisting of i) an erythropoietin that lacks sialic acid moieties, ii) an erythropoietin having at least no sialic acid moieties; iii) an erythropoietin having at least no N-linked or no O-linked carbohydrates; iv) an erythropoietin having at least a reduced carbohydrate content by virtue of treatment of native erythropoietin with at least one glycosidase; v) an erythropoietin having at least one or more oxidized carbohydrates; vi) an erythropoietin having at least one or more oxidized carbohydrates and is chemically reduced; vii) an erythropoietin having at least one or more modified arginine residues; viii) an erythropoietin having at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule; ix) an erythropoietin having at least a modified tyrosine residue; x) an erythropoietin having at least a modified aspartic acid or a glutamic acid residue; xi) an erythropoietin having at least a modified tryptophan residue; xii) an erythropoietin having at least one amino group removed; xiii) an erythropoietin having at least an opening of at least one of the cystine linkages in the erythropoietin molecule; or xiv) a truncated erythropoietin.

14. The method of claim 13, wherein the chemically modified erythropoietin lacks erythropoietin's erythropoietic effects.

15. The method of claim 14, wherein the chemically modified erythropoietin comprises carbamylated erythropoietin.

16. The method of claim 12, wherein the mutated erythropoietin is selected from the group consisting of one or more of the following mutations C7S, R10I, V11S, L12A, E13A, R14A, R14B, R14E, R14Q, Y15A, Y15F, Y15I, K20A, K20E, E21A, C29S, C29Y, C33S,

C33Y, P42N, T44I, K45A, K45D, V46A, N47A, F48A, F48I, Y49A, Y49S, W51F, W51N, Q59N, E62T, L67S, L70A, D96R, K97D, S100R, S100E, S100A, S100T, G101A, G101I, L102A, R103A, S104A, S104I, L105A, T106A, T106I, T107A, T107L, L108K, L108A, S126A, F142I, R143A, S146A, N147K, N147A, F148Y, L149A, R150A, G151A, K152A, L153A, L155A, C160S, I6A, C7A, B13A, N24K, A30N, H32T, N38K, N83K, P42A, D43A, K52A, K97A, K116A, T132A, I133A, T134A, K140A, P148A, R150B, G151A, K152W, K154A, G158A, C161A, and/or R162A.

17. The method of claim 16, wherein the mutated erythropoietin lacks erythropoietin's erythropoietic effects.

18. The method of claim 11, wherein the condition associated with the effects of proinflammatory cytokines comprises sepsis, adhesions, wounds, inflammation or chronic disease.

19. A pharmaceutical composition comprising an amount of at least one tissue protective cytokine effective in treating, preventing, delaying the onset of, or reducing the effects of proinflammatory cytokines in a mammal.

20. The pharmaceutical composition of claim 19, wherein the at least one tissue protective cytokine comprises a chemically modified erythropoietin or mutated erythropoietin.

21. The pharmaceutical composition of claim 20, wherein the the chemically modified erythropoietin is selected from the group consisting of i) an erythropoietin that lacks sialic acid moieties, ii) an erythropoietin having at least no sialic acid moieties; iii) an erythropoietin having at least no N-linked or no O-linked carbohydrates; iv) an erythropoietin having at least a reduced carbohydrate content by virtue of treatment of native erythropoietin with at least one glycosidase; v) an erythropoietin having at least one or more oxidized carbohydrates; vi) an erythropoietin having at least one or more oxidized carbohydrates and is chemically reduced; vii) an erythropoietin having at least

one or more modified arginine residues; viii) an erythropoietin having at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule; ix) an erythropoietin having at least a modified tyrosine residue; x) an erythropoietin having at least a modified aspartic acid or a glutamic acid residue; xi) an erythropoietin having at least a modified tryptophan residue; xii) an erythropoietin having at least one amino group removed; xiii) an erythropoietin having at least an opening of at least one of the cystine linkages in the erythropoietin molecule; or xiv) a truncated erythropoietin.

22. The pharmaceutical composition of claim 21, wherein the chemically modified erythropoietin lacks erythropoietin's erythropoietic effects.

23. The pharmaceutical composition of claim 22, wherein the chemically modified erythropoietin comprises carbamylated erythropoietin.

24. The pharmaceutical composition of claim 20, wherein the mutated erythropoietin is selected from the group consisting of one or more of the following mutations C7S, R10I, V11S, L12A, E13A, R14A, R14B, R14E, R14Q, Y15A, Y15F, Y15I, K20A, K20E, E21A, C29S, C29Y, C33S, C33Y, P42N, T44I, K45A, K45D, V46A, N47A, F48A, F48I, Y49A, Y49S, W51F, W51N, Q59N, E62T, L67S, L70A, D96R, K97D, S100R, S100E, S100A, S100T, G101A, G101I, L102A, R103A, S104A, S104I, L105A, T106A, T106I, T107A, T107L, L108K, L108A, S126A, F142I, R143A, S146A, N147K, N147A, F148Y, L149A, R150A, G151A, K152A, L153A, L155A, C160S, I6A, C7A, B13A, N24K, A30N, H32T, N38K, N83K, P42A, D43A, K52A, K97A, K116A, T132A, I133A, T134A, K140A, P148A, R150B, G151A, K152W, K154A, G158A, C161A, and/or R162A.

25. The pharmaceutical composition of claim 24, wherein the mutated erythropoietin lacks erythropoietin's erythropoietic effects.

26. The pharmaceutical composition of claim 19 wherein the proinflammatory cytokine comprises an Interleukin or TNF.

27. The pharmaceutical composition of claim 26 wherein the proinflammatory cytokine is TNF.

28. The pharmaceutical composition of claim 19 wherein the effect of the proinflammatory cytokine comprises fever, wasting, lethargy, anemia, edema, ischemia, organ failure and insulin resistance.

29. A pharmaceutical composition comprised of an amount of at least one tissue protective cytokine effective in treating, preventing, delaying the onset of a condition associated with proinflammatory cytokines in a mammal.

30. The pharmaceutical composition claim 29, wherein the at least one tissue protective cytokine comprises a chemically modified erythropoietin or mutated erythropoietin.

31. The pharmaceutical composition claim 30, wherein the the chemically modified erythropoietin is selected from the group consisting of i) an erythropoietin that lacks sialic acid moieties, ii) an erythropoietin having at least no sialic acid moieties; iii) an erythropoietin having at least no N-linked or no O-linked carbohydrates; iv) an erythropoietin having at least a reduced carbohydrate content by virtue of treatment of native erythropoietin with at least one glycosidase; v) an erythropoietin having at least one or more oxidized carbohydrates; vi) an erythropoietin having at least one or more oxidized carbohydrates and is chemically reduced; vii) an erythropoietin having at least one or more modified arginine residues; viii) an erythropoietin having at least one or more modified lysine residues or a modification of the N-terminal amino group of the erythropoietin molecule; ix) an erythropoietin having at least a modified tyrosine residue; x) an erythropoietin having at least a modified aspartic acid or a glutamic acid residue; xi) an erythropoietin having at least a modified tryptophan residue; xii) an erythropoietin

having at least one amino group removed; xiii) an erythropoietin having at least an opening of at least one of the cystine linkages in the erythropoietin molecule; or xiv) a truncated erythropoietin.

32. The pharmaceutical composition of claim 31, wherein the chemically modified erythropoietin lacks erythropoietin's erythropoietic effects.

33. The pharmaceutical composition of claim 32, wherein the chemically modified erythropoietin comprises carbamylated erythropoietin.

34. The pharmaceutical composition of claim 30, wherein the mutated erythropoietin is selected from the group consisting of one or more of the following mutations C7S, R10I, V11S, L12A, E13A, R14A, R14B, R14E, R14Q, Y15A, Y15F, Y15I, K20A, K20E, E21A, C29S, C29Y, C33S, C33Y, P42N, T44I, K45A, K45D, V46A, N47A, F48A, F48I, Y49A, Y49S, W51F, W51N, Q59N, E62T, L67S, L70A, D96R, K97D, S100R, S100E, S100A, S100T, G101A, G101I, L102A, R103A, S104A, S104I, L105A, T106A, T106I, T107A, T107L, L108K, L108A, S126A, F142I, R143A, S146A, N147K, N147A, F148Y, L149A, R150A, G151A, K152A, L153A, L155A, C160S, I6A, C7A, B13A, N24K, A30N, H32T, N38K, N83K, P42A, D43A, K52A, K97A, K116A, T132A, I133A, T134A, K140A, P148A, R150B, G151A, K152W, K154A, G158A, C161A, and/or R162A.

35. The pharmaceutical composition of claim 34, wherein the mutated erythropoietin lacks erythropoietin's erythropoietic effects.

36. The pharmaceutical composition of claim 29, wherein the condition associated with the effects of proinflammatory cytokines comprises sepsis, adhesions, wounds, inflammation or chronic disease.